

Express Mail No.: EV719390015US
International Application No.: PCT/US2004/007451
International Filing Date: 10 March 2004
Preliminary Amendment

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1.-4. (Cancelled)

5. (New) A method for detecting the presence of lung cancer cells in a biological sample comprising the steps of:

- (a) detecting the level of mRNA expression in the biological sample of two or more cancer-associated markers selected from the group consisting of L762P, L550S, L587S, L984P, L552S, and L763P; and
- (b) comparing the level of mRNA expression detected in the biological sample for each marker to a predetermined cut-off value for each marker;

wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the biological sample.

6. (New) A method for detecting the presence of lung cancer cells in a biological sample comprising the steps of:

- (a) detecting the level of mRNA expression in the biological sample of two or more cancer-associated markers selected from the group consisting of L762P, L550S, L587S, and L984P; and
- (b) comparing the level of mRNA expression detected in the biological sample for each marker to a predetermined cut-off value for each marker;

wherein a detected level of expression above the predetermined cut-off value for one or more markers is indicative of the presence of lung cancer cells in the biological sample.

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7. (New) The method of claim 6, wherein step (a) comprises detecting the level of mRNA expression using a nucleic acid hybridization technique.

8. (New) The method of claim 6, wherein step (a) comprises detecting the level of mRNA expression using a nucleic acid amplification method.

9. (New) The method of claim 8, wherein step (a) comprises detecting the level of mRNA expression using a nucleic acid amplification method selected from the group consisting of transcription-based amplification, polymerase chain reaction amplification (PCR), ligase chain reaction amplification (LCR), strand displacement amplification (SDA), and nucleic acid sequence based amplification (NASBA).

10. (New) The method of claim 6, wherein the L762P cancer-associated marker comprises a nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2.

11. (New) The method of claim 6, wherein the L550S cancer-associated marker comprises a nucleic acid sequence set forth in SEQ ID NO: 5 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 6.

12. (New) The method of claim 6, wherein the L587S cancer-associated marker comprises a nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 27.

13. (New) The method of claim 6, wherein the L984P cancer-associated marker comprises a nucleic acid sequence set forth in SEQ ID NO: 3 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4.

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14. (New) The method of claim 6, wherein the cancer is a small cell lung cancer or a non-small cell lung cancer.

15. (New) The method of claim 6, wherein the biological sample is a sample suspected of containing cancer-associated markers or cancer cells expressing such markers.

16. (New) The method of claim 15, wherein the biological sample is selected from the group consisting of a biopsy sample, lavage sample, sputum sample, serum sample, peripheral blood sample, lymph node sample, bone marrow sample, urine sample, and pleural effusion sample.

17. (New) A composition for detecting cancer cells in a biological sample comprising two or more of:

- a) a first oligonucleotide that specifically hybridizes to L762P;
- b) a second oligonucleotide that specifically hybridizes to L550S;
- c) a third oligonucleotide that specifically hybridizes to L587S; and
- d) a fourth oligonucleotide that specifically hybridizes to L984P.

18. (New) The composition of claim 17, wherein the first oligonucleotide specifically hybridizes to an L762P nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2, the second oligonucleotide specifically hybridizes to an L550S nucleic acid sequence set forth in SEQ ID NO: 5 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 6, the third oligonucleotide specifically hybridizes to an L587S nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 27, and the fourth oligonucleotide specifically hybridizes to an L984P nucleic acid sequence set forth in

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SEQ ID NO: 3 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4.

19. (New) A diagnostic kit for detecting cancer cells in a biological sample comprising two or more of:

- a) a first oligonucleotide that specifically hybridizes to L762P;
- b) a second oligonucleotide that specifically hybridizes to L550S;
- c) a third oligonucleotide that specifically hybridizes to L587S; and
- d) a fourth oligonucleotide that specifically hybridizes to L984P.

20. (New) The kit of claim 19, wherein the first oligonucleotide specifically hybridizes to an L762P nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2, the second oligonucleotide specifically hybridizes to an L550S nucleic acid sequence set forth in SEQ ID NO: 5 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 6, the third oligonucleotide specifically hybridizes to an L587S nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 27, and the fourth oligonucleotide specifically hybridizes to an L984P nucleic acid sequence set forth in SEQ ID NO: 3 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4.

21. (New) A composition for detecting cancer cells in a biological sample comprising two or more of:

- a) a first primer pair that specifically hybridizes to L762P;
- b) a second primer pair that specifically hybridizes to L550S;
- c) a third primer pair that specifically hybridizes to L587S; and
- d) a fourth primer pair that specifically hybridizes to L984P.

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22. (New) The composition of claim 21, wherein the first, second, third and fourth primer pairs are effective in a nucleic acid amplification method for amplifying all or a portion of an L762P nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2, an L550S nucleic acid sequence set forth in SEQ ID NO: 5 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 6, an L587S nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 27, and an L984P nucleic acid sequence set forth in SEQ ID NO: 3 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4, respectively.

23. (New) A diagnostic kit for detecting cancer cells in a biological sample comprising two or more of:

- a) a first primer pair that specifically hybridizes to L762P;
- b) a second primer pair that specifically hybridizes to L550S;
- c) a third primer pair that specifically hybridizes to L587S; and
- d) a fourth primer pair that specifically hybridizes to L984P.

24. (New) The kit of claim 23, wherein the first, second, third and fourth primer pairs are effective in a nucleic acid amplification method for amplifying all or a portion of an L762P nucleic acid sequence set forth in SEQ ID NO: 1 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 2, an L550S nucleic acid sequence set forth in SEQ ID NO: 5 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 6, an L587S nucleic acid sequence set forth in SEQ ID NO: 26 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 27, and an L984P nucleic acid sequence set forth in SEQ ID NO: 3 or a nucleic acid sequence encoding an amino acid sequence set forth in SEQ ID NO: 4, respectively.

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25. (New) A diagnostic kit for detecting cancer cells in a biological sample comprising two or more of:

- a) a first antibody specific for an L762P protein;
- b) a second antibody specific for an L550S protein;
- c) a third antibody specific for an L587S protein; and
- d) a fourth antibody specific for an L984P protein.

26. (New) The kit of claim 25, wherein the L762P protein comprises an amino acid sequence set forth in SEQ ID NO: 2, the L550S protein comprises an amino acid sequence set forth in SEQ ID NO: 6, the L587S protein comprises an amino acid sequence set forth in SEQ ID NO: 27, and the L984P protein comprises an amino acid sequence set forth in SEQ ID NO: 4.